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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/202,104	04/30/1999	LEONARDUS ADRIANUS MARIA VAN LEENGOED	3890US	2481

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EXAMINER	
LANDSMAN, ROBERT S	
ART UNIT	PAPER NUMBER
1647	19

DATE MAILED: 01/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/202,104	VAN LEENGOED ET AL.	
	Examiner	Art Unit	
	Robert Landsman	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-6,8-12,15-17,19,21-23,47 and 71-86* is/are pending in the application.

4a) Of the above claim(s) *10,19,47,73,76,77,79,80 and 82-85* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-6,8,9,11,12,15-17,21-23,71,72,74,75,78,81 and 86* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence Comparisons A and B* .

DETAILED ACTION

1. Formal Matter

A. Amendment E, filed 7/30/02, has been entered into the record.

B. Claims 1, 4-6, 8-12, 15-17, 19, 21-23, 47 and 71-73 were pending in the application. New claims 74-86 have been added. Claims 10, 19, 47, 73, 76, 77, 79, 80 and 82-85 have been withdrawn as being drawn to a non-elected invention. Therefore, claims 1, 4-6, 8, 9, 11, 12, 15-17, 21-23, 71, 72, 74, 75, 78, 81 and 86 are the subject of this Office Action.

C. All Statutes not found in this Office Action can be found, cited in full, in a previous Office Action.

2. Specification

A. The objection to the title has been withdrawn in view of Applicants' arguments that certain peptides have agonistic activity.

B. The objection to the specification has been withdrawn since Applicants have provided a Brief Description of the Drawings.

C. The specification is objected to since the priority claim (i.e. CROSS-REFERENCE TO RELATED APPLICATIONS) to PCT/NL97/00345 is not recited in the first line of the specification.

D. The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.

(d) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC (See 37 CFR 1.52(e)(5) and MPEP 608.05. Computer program listings (37 CFR 1.96(c)), "Sequence Listings" (37 CFR 1.821(c)), and tables having more than 50 pages of text are permitted to be submitted on compact discs.) or
REFERENCE TO A "MICROFICHE APPENDIX" (See MPEP § 608.05(a). "Microfiche Appendices" were accepted by the Office until March 1, 2001.)

(e) BACKGROUND OF THE INVENTION.
(1) Field of the Invention.
(2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.

(f) BRIEF SUMMARY OF THE INVENTION.

(g) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).

(h) DETAILED DESCRIPTION OF THE INVENTION.

(i) CLAIM OR CLAIMS (commencing on a separate sheet).

(j) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).

(k) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

E. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

3. Claim Objections

A. All claim objections have been withdrawn in view of Applicants' arguments or amendments to the claims.

4. Claim Rejections - 35 USC § 101

A. The rejection of claim 1 under 35 USC 101 regarding "the hand of man" has been withdrawn in view of Applicants' amendment to the claim.

B. The rejection of claims 17, 21 and 24 under 35 USC 101 regarding reciting a use without setting forth method steps has been withdrawn in view of Applicants' amendments to the claims. However, new issues regarding these claims have been raised as seen in the following rejections.

5. Claim Rejections - 35 USC § 112, first paragraph - enablement

A. Claims 1, 4-6, 8, 9, 11, 12, 15-17, 21-23, 71 and 72 remain rejected and new claim 74, 75, 78, 81 and 86 are also rejected under 35 USC 112, first paragraph, for the reasons already of record in the Office Action dated 1/30/02. Applicants argue that the specification does provide sufficient guidance for one of ordinary skill in the art to determine whether a peptide exhibits antagonistic activity against IL-6 by using, for example, a proliferation assay, or other assays disclosed in the specification. These arguments have been considered, but are not deemed persuasive.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

First, the breadth of the claims is excessive regarding Applicants claiming any peptide comprising 5-30 residues of SEQ ID NO:11, or 5-20 residues of SEQ ID NO:5. This would allow for hundreds of peptides to be encompassed by the claims and Applicants have not provided any guidance or working examples of peptides of 5-30 residues, other than SEQ ID NO:5 and 11, which are IL-6 antagonists. A disclosure of the critical residues required to produce a peptide which is an IL-6 antagonist is missing and it is not predictable to the artisan which residues of SEQ ID NO:5 or 11 would be required in order to produce a peptide which is an antagonist to IL-6. In other words, the artisan would not know which regions of SEQ ID NO:5 or 11 to use to produce these antagonists.

Therefore, in summary, the breadth of the claims is excessive with regard to Applicants claiming potentially hundreds of IL-6 antagonists. Applicants have only provided guidance and working examples of 2 antagonists. This coupled with the lack of predictability as to what residues are critical to produce an IL- antagonist, leads the Examiner to hold that undue experimentation is required to practice the invention as claimed.

B. Claims 15-17, 22, 23, 74, 78, 81 and 86 are rejected under 35 USC 112, first paragraph, because the specification, while being enabling for compositions comprising IL-6 antagonists and a proliferation assay to identify IL-6 antagonists in vitro, does not reasonably provide enablement for pharmaceutical compositions comprising IL-6 antagonists and methods of using IL-6 antagonists in vivo, or methods for manufacturing medicaments. The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

First, the breadth of the claims is excessive since the claims read on all pharmaceutical compositions comprising an IL-6 antagonist to treat all diseases. Applicants have provided no guidance or working examples of any methods of treatment for any diseases using this protein, or for clearing blood or blood products of IL-6 using an IL-6 antagonist. The only assays disclosed in the specification are a proliferation assay and an acute-phase reaction assay and no nexus has been disclosed between any in vitro data and in vivo results. Furthermore, it is not predictable to one of ordinary skill in the art how to use a pharmaceutical composition. Applicants can overcome the rejection of any claims reciting "pharmaceutical composition" by amending the claims to recite, for example, "a composition comprising the...of claim 1 and an inert carrier" **without adding new matter**. Similarly, claims 16 and 81 read on in vivo treatment. Regardless, Applicants have not taught how to clear IL-6 from the blood by using on IL-6 antagonist. This antagonist could be used to remove IL-6 receptor molecules from the blood since these would likely bind to the receptor, but it is unclear how one would be able to remove IL-6 itself. In addition, claim 74 reads on in vivo treatment and Applicants have not taught any methods for exerting IL-6 activity in vivo.

In summary, the breadth of the claims is excessive with regard to Applicants claiming pharmaceutical compositions and their use in treating any and all IL-6-related diseases.. There is also a lack of guidance and working examples of how to use these compositions, including how to clear blood and blood products. These factors, along with the lack of predictability to one of ordinary skill in the art as to how to use pharmaceutical compositions comprising these IL-6 antagonists, leads the Examiner to hold that undue experimentation is necessary to practice the invention as claimed.

6. Claim Rejections - 35 USC § 112, second paragraph

A. All rejections under 35 USC 112, second paragraph, have been withdrawn in view of Applicants' arguments, or amendments to the claims. However, new rejections are recited below.

B. Claims 16, 17, 21, 74, 81 and 86 rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: providing steps for the artisan to perform the recited methods. Claims 16 and 81 recite clearing blood or blood products of IL-6. However, the claim only recites contacting

products with a peptide. This step itself, respectfully, does not clear the blood or blood products. Similarly, there is no conclusory step reciting that the goal has been achieved, such as "wherein said molecules have been cleared. A similar format needs to be followed for claims 17, 21, 74 and 86. For example, claim 17 does not recite how the disease is to be treated, or how to know when the disease has been treated. The only step is administering a peptide.

7. Claim Rejections - 35 USC § 102

A. All rejections under 35 USC 102 have been withdrawn in view of Applicants' amendment to the claims to recite SEQ ID NO:11

8. Closest Prior Art

A. No prior art recites a peptide of 5-30 residues of SEQ ID NO:5 or 11 with IL-6 activity. However, both Daicel Chem Ind Ltd (Accession No. AAW00403; Sequence Comparison A) and Yamasaki et al. (Accession No. A41242; Sequence Comparison B) teach peptides which are larger than 30 residues of SEQ ID NO:5 and 11.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
January 14, 2003